Message

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Sent: 1/26/2022 5:42:40 PM
To: Reynolds, Alan [Reynolds.Alan@epa.gov]; Striegel, Wiebke [Striegel.Wiebke@epa.gov]
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Subject: OX5034 Label Claims / Efficacy Measure

Hi Alan and Wiebke,

Per our conversation yesterday on the OX5034 EUP extension/amendment regarding whether the correct measures of efficacy are being assessed, I've written up a quick summary as to why mating fraction is the end point and not adult female population level.

You both raised that Oxitec should be measuring adult female mosquito population suppression, like MosquitoMate (MM) did, to standardize all modified mosquito products. However, the claims being made between Oxitec and MM differ. Oxitec wants to make larvicidal control claims, while MM wanted to make adult mosquito population suppression claims. So, we have two different end points between the two EUPs because the intended label claims are different.

Amanda, Eric, and Oxitec had many conversations about using larvicidal claims versus adult population suppression claims. Overall it was determined that mating fraction could provide a measure of the effectiveness of the product as a larvicide and get at population suppression as well.

The Section G currently has the below three efficacy measures as stated by Oxitec. I've pasted the Oxitec measures below, and in sub-bullets, ETB thoughts on these measures:

- Efficacy of the active ingredient (% mortality observed in fluorescent female progeny compared untreated, i.e. non-fluorescent females).
    - ETB has told Oxitec that measuring efficacy of the AI, essentially a proof of concept, is not the same as the efficacy of the product. While Oxitec will be measuring this, it's unlikely to be the efficacy endpoint for the Section 3 label claims.
- The adult over-flooding ratio or sex ratio achieved i.e. Oxitec males:wild male ratio and/or male:female ratio (using adult traps).
- The proportion of treated i.e. fluorescent individuals within ovitraps (mating fraction).
    - ETB and Oxitec determined mating fraction is the best way to estimate efficacy given the claims are for larvicidal control.
    - In the treated area, an increased proportion of fluorescent larvae over time indicates a reduction in the breeding population of wild type females. Eventually, there may be all fluorescent larvae in ovitraps or if the product works really well – no larvae at all. Mating fraction can be compared between control and treatment areas as well.

In the original EUP Section G, Oxitec had a section called "2. Proposed Claims to be Supported by Field Trials" which is not in the new amendment/extension Section G which got at the efficacy measurements somewhat, although largely tried to justify why efficacy of the AI was the best measure. In ETB's review of the original Section G, we stated that the final efficacy endpoint will be evaluated at the time of Section 3 registration, but that there's a preference for mating fraction as the endpoint.

Hopefully this makes why Oxitec has the endpoints they have and why they aren't the same as MM more clear. Essentially it's because the claims are different.

Thanks,

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